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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,280	12/29/2000	D. Scott Wilbur	33700WC005	6495

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,280	WILBUR ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,73,74 and 99-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *34, 73-74, 99-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/13/2005 has been entered.

The amendment filed on 12/13/2005 amended claims 34, 73, and 74, and added new claims 99-112. Amendment also cancelled claims 36, and 38.

Applicant's amendment by limiting the disease to myocardial infarcts, myocardial perfusion, and cancer is sufficient to overcome the rejection of claims 73 and 74 under 112, first paragraph.

Applicant's amendment by canceling claims 36 and 38 is sufficient to overcome the rejection of claims 36, and 38 under 35 U.S.C. 103(a) as being unpatentable Wilbur et al. and Rosebrough, and further in view of Griffiths (5,482,698).

Claims 34, 73-74, 99-112 are pending, and examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 112 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claim recites the limitation "wherein the reagent is selected from the group consisting of", and the omitted elements are the reagents.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "reagent comprises" is vague and indefinite, as the metes and bound of this claim is unascertainable. In claim 99 the reagent is defined as a single molecule. How can a single molecule comprise more compounds?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34, 73-74, 99, 100-107, 109-112 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilber et al. (WO 97/29114, PTO-1449 of record).

Wilbur et al. discloses biotin-containing reagent, and biotinylation reagents incorporate soluble linker moieties. Exemplified is a trifunctional reagent comprising tricarboxybenzene, biotin as the affinity ligand, maleimide as the biomolecule reactive moiety, iodinated benzene as the effector agent, and trioxadiamine as linker 1, linker 2, and linker 3. Affinity ligand, biotin is attached to trifunctional moiety through linker which has a length of at least 9 angstoms. See page 17, lines 26-30; page18, lines1-12; and pages 38-39. The water soluble linker moieties include groups such as ethers, carboxylates, sulfonates, ammonium etc., and with preferably 8 to 20 atoms in length. See pages 8-9. Biotin-containing compounds that are chelatable to radionuclides such as In-111, Y-90, Ga-67, Ga-68, Cu-64, Cu-67, Sm-153,, Tc-99, Tc-99m, Re-186, Re-188 are disclosed. It is also disclosed that the radionuclides, gamma imaging radionuclides and therapeutic radionuclides are bound via chelation to amino-carboxy derivatives such as EDTA, DTPA, and cyclic amines such as NOTA, DOTA, and TETA. See page 23, lines 1-15. Biotin-containing compounds activated esters such as hydroxysuccinimidyl, hydroxybenztriazole, N-hydroxypyrrolidone, phenyl, 2- and 4-nitrophenyl etc. are disclosed. See page 18, lines 14-30. The water soluble linker may be coupled to a biotin moiety through an amide forming reaction employing a amine group on the linker and the carboxylate site on a biotin moiety. The amide forming reaction may include the use of coupling agents. Wilbur further teaches that the linker moiety attached to the biotin moiety is modified under certain conditions by introduction of a steric group such as carboxylates, larger alkyl groups, aryl groups etc. alpha to the amine (or another functionality) of the linker, to provide resistance to cleavage by

biotindase. Modifications of biotin by conjugation with water soluble linkers possessing a branched chain alpha methyl group such as a 3-aminobutyric acid, 1,2-diaminopropane, are desirable to produce conjugates more resistant to *in vivo* degradation by the enzyme biotinidase. Wilbur teaches that by combining a variety of biotin moieties with the carboxylate coupled steric moieties and a water soluble linker moiety, water soluble biotin compounds having varying binding affinities with biotin-binding proteins and enhanced resistance to *in vivo* degradation are obtained.

The limitation drawn to the intended use of the instant reagent has not been given any patentable weight i.e "for conjugation to a biomolecule" in claim 99, "for diagnosis of a disease in a mammal" in claim 73, "for treatment of a cancer" in claim 74 because the recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

The recitation "for conjugation to a biomolecule with minimal perturbation of said biomolecule" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d

67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*. 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

It is further noted that the binding affinity of a molecule is a property of the said molecule. Accordingly, since Wilbur et al. disclose the same affinity ligands as instantly claimed, absent evidence to the contrary, the compounds will have the same binding affinities as instantly claimed. A product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 108 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wilber et al. (WO 97/29114) as applied to claims 34, 73-74, 99, 100-107, 109-112, and further in view of Rosebrough (The Journal of Pharmacology and Experimental Therapeutics, vol 265, No.1, 1993, 408-415).

Wibur et al. is as discussed above.

Wilbur et al. does not teach "aspartyl group" in linker 1 of the affinity ligand, biotin.

Rosebrough teaches the pharmacokinetics, and *in vivo* and *in vitro* stability of radiolabeled deferoxamine-biotin derivatives in plasma. See abstract. Rosebrough teaches that introduction of a carboxyl group alpha to the amide bond of biotinamide, blocks the biotinidase activity, thereby increasing the stability of biotinamide bond towards enzymatic cleavage and also the binding ability towards avidin *in vivo* and *in vitro* is still maintained. See page 410; page 414, lines 35-40.

From the teachings of Wilber and Rosebrough, it would have been obvious to one having ordinary skill in the art at the time the invention was made, to use aspartyl moiety in linker 1 of the affinity ligand because (1) Rosebrough teaches that by introducing an alpha carboxylate group to the amide bond in the linker 1 increases stability towards enzymatic cleavage, thus by introducing an aspartyl moiety in linker 1 introduces a beta carboxylate group to the amide bond in the linker 1, which is a homologue of alpha carboxylate, 2) a homologous series is a family of chemically related compounds, the composition of which varies from member to member by CH_2 * * *, wherein Chemists knowing the properties of one member would in general know what to expect in adjacent members (In re Henze, 85 USPQ 261, 261 (CCPA 1950)); thus, one of skill in the art would have been motivated to teach "Aspartyl moiety" as alpha-carboxylate in linker 1 a) because of the expectation of achieving the same binding with avidin or streptavidin and b) because adjacent homologs are considered to be obvious variants absent unexpected results.

Response to Arguments

Applicant's arguments with respect to rejection of claims under 103(a) have been considered but are moot in view of the new ground(s) of rejection, but are address, as applicable, below.

Applicant's argument "Neither Wilbur nor Rosebrough teaches or suggests that binding a radionuclide via chelation to linker 2 to a general structure (I) in claim 99 results in a more stable reagent, wherein the biotin is separated from the rest of the reagent through a linker 1 having a length of at least 9 angstroms." This argument is not persuasive because 1) it is not commensurate in scope with the instant claims which are directed to a single molecule reagent, and not to the properties such as stability of the reagent, 2) Wilbur et al. discloses biotin-containing reagent, and biotinylation reagents which incorporate soluble linker moieties, and further teaches that biotin-containing reagent is obtained by attaching an affinity ligand, biotin, a biomolecule reactive moiety, maleimide, and an effector agent, to trifunctional molecule, tricarboxybenzene through linkers such as trioxadiamine. Wibur as discussed above further discloses that the effector agent can be a radionuclide binding/bonding moieties that bind the radionuclides, gamma imaging radionuclides and therapeutic radionuclides via chelation to amino-carboxy derivatives such as EDTA, DTPA, and cyclic amines such as NOTA, DOTA, and TETA. See page 23, lines 1-15. Wilbur also discloses that the affinity ligand, biotin is attached to trifunctional moiety through linker which has a length of at least 9 angstoms. Thus, the reagent taught by Wibur anticipates the instant disclosed reagent.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 7.30am-3.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER